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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,122	12/03/2003	David R. Cox	UCSF-127CON2	7640

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	PAPER NUMBER
1637	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/19/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/728,122	COX ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-30,33 and 35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-30,33 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Interpretation

1. The only term at issue in the current case is the impact of the word "kit". The specification discusses "kits" at page 23, lines 17-27, but does not require any specific structure for a "kit". That is, the specification does not envision that a "kit" is in a box, or is composed of microfuge tubes, or has any specific structure. Therefore, prior art which teaches the claimed compositions necessarily teaches the "kit", since these compositions are structurally identical to the "kit" as per MPEP 2112.01 (III).

Priority

2. This application claims priority to 08/713,751. A review of that application fails to identify any support for claims 34 and 35. Therefore, these claims are accorded benefit of priority only to March 17, 1999 of the 09/271,055 application.

Claim Rejections - 35 USC § 112

The rejection of claims 34 and 35 under 35 U.S.C. 112, second paragraph, is withdrawn in view of the amendment.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 26-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Parker et al (Proc. Natl. Acad. Sci. (1992) 89:1730-1734.

Parker teaches a kit comprising:

(a) a first DNA vector comprising a gene encoding a detectable marker, an origin of replication active in a bacterial host cell and a sequence of interest, wherein said vector lacks methyl adenine (see page 1730, column 2, where the pPY97 vector has a detectable marker that is the mnt gene, a bacterial origin of replication active in E. coli (see page 1731, column 1, paragraph after "results" discusses M13 origin of replication), and other sequences which can be of interest to someone, and where the vector is grown in the GM1690 E. coli host strain so that the vector lacks methyl adenine),

(b) a second DNA vector that is substantially complementary which has an mnt gene with an inactivating deletion of 5 nucleotides and which comprises methyl adenine at GATC sites (see page 1730, column 2, where the pPY97 vector with the 5 nucleotide deletion is grown in the JC9239 E. coli host cell which results in methylated vector DNA).

(c) Parker teaches competent host bacteria including GM4388, which is based on GM 4331 which is an MMR strain, where GM4388 has Tn5 which transposon has the antibiotic resistance Gene Kanamycin and which is inherently sensitive to other antibiotics (see page 1731, column 1, first paragraph).

With regard to claim 27, the pPY97 vector of Parker comprises a selectable marker that is ampicillin resistance gene (see page 1731, column 1) and the pBR322 polylinker (see page 1731, column 1).

With regard to claims 28 and 29, Parker teaches single stranded pPY mutant and wildtype (see page 1730, column 2, last paragraph).

With regard to claim 30, Parker teaches annealing of the two vectors (see page 1730, column 2, last paragraph).

5. Claims 26-30, 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Carraway et al (J. Bacteriol. (1993) 175:3972-3980).

Carraway teaches a kit comprising:

(a) a first DNA vector comprising a gene encoding a detectable marker, an origin of replication active in a bacterial host cell and a sequence of interest, wherein said vector lacks methyl adenine (see page 3973, column 1, where the pPY97 vector has a detectable marker that is the mnt gene, a bacterial origin of replication active in E. coli (see page 3973, column 1 discusses M13 origin of replication), and other sequences which can be of interest to someone, and where the vector is grown in the GM1690 E. coli host strain so that the vector lacks methyl adenine (see page 3973, column 2),

(b) a second DNA vector that is substantially complementary which has an mnt gene with an inactivating deletion of 5, 192, or 410 nucleotides and which comprises methyl adenine at GATC sites (see page 3973, columns 1 and 2, where the pPY97 vectors with the deletions are grown in the JC9239 E. coli host cell which results in methylated vector DNA (see page 3973, column 2).

(c) Carroway teaches competent host bacteria including GM4388, which is based on GM 4331 which is an MMR strain, where GM4388 has Tn5 which

transposon has the antibiotic resistance Gene Kanamycin and which is inherently sensitive to other antibiotics (see page 3974, table 1).

With regard to claim 27, the pPY97 vector of Carraway comprises a selectable marker that is ampicillin resistance gene (see page 3974, column 2) and the pBR322 polylinker (see page 3973, column 1).

With regard to claims 28 and 29, Carraway teaches single stranded pPY mutant and wildtype (see page 3973, column 2).

With regard to claim 30, Carraway teaches annealing of the two vectors (see page 3973, column 2).

With regard to claims 31, 32, Carraway teaches competent host bacteria including GM4331 which is an MMR strain (see page 3973, columns 1 and 2, subheading "Bacterial strains").

With regard to claim 33, Carraway teaches the use of two oligonucleotides and the T7 DNA polymerase, which is "thermostable" as broadly interpreted (see page 3973, column 1).

6. Claims 26, 27, 34 and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Sternberg et al (J. Mol. Biol. (1986) 187:197-212).

Sternberg teaches a "kit" comprising:

(a) a first DNA vector, PK01-2368 delta 100 (see page 203, table 2 and page 208, table 5) comprising a gene encoding a detectable marker, an origin of replication active in a bacterial host cell and a sequence of interest, wherein said vector lacks methyl adenine (First see page 198, column 1, where the starting

pRH43 plasmids have the PBR322 origin of replication that is active in bacterial cells and the ampicillin detectable marker, then see page 199, figure 1, where the chimeric P1 plasmids have LoxP and Cre sequences of interest) and where the vector is grown in dam + and dam – cells (see page 208, table 5),

(b) a second DNA vector, PK011-103 delta 77 (see page 203, table 2 and page 208, table 5) that is substantially complementary to PK01-2368 delta 100 (which is inherent since both share the entire plasmid except for part of the CRE promoter elements) comprising a gene encoding a detectable marker, an origin of replication active in a bacterial host cell and a sequence of interest, wherein said vector lacks methyl adenine (First see page 198, column 1, where the starting pRH43 plasmids have the PBR322 origin of replication that is active in bacterial cells and the ampicillin detectable marker, then see page 199, figure 1, where the chimeric P1 plasmids have LoxP and Cre sequences of interest) and where the vector is grown in dam + and dam – cells (see page 208, table 5),

(c) Sternberg teaches competent host bacteria including NS2626 which is an MMR strain, where NS2626 has Tn9 which transposon has the antibiotic resistance Gene Chloramphenicol and which is inherently sensitive to other antibiotics (see page 198, table 1 and column 1).

With regard to claim 27, the PK01-2368 delta 100 vector of Sternberg comprises a selectable marker that is ampicillin resistance gene (see page 198, column 1) and the pBR322 polylinker (see page 198, column 1).

With regard to claims 31, 32, Sternberg teaches competent host bacteria including N99 and NS2626 which is an MMR strain (see table 5 legend).

With regard to claims 34 and 35, Sternberg teaches detection of the Cre-Lox genes (see table 5).

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Carraway et al (J. Bacteriol. (1993) 175:3972-3980) in view of Zambrowicz (U.S. Patent 6,080,576).

Carraway teaches a kit comprising:

(a) a first DNA vector comprising a gene encoding a detectable marker, an origin of replication active in a bacterial host cell and a sequence of interest, wherein said vector lacks methyl adenine (see page 3973, column 1, where the pPY97 vector has a detectable marker that is the mnt gene, a bacterial origin of replication active in E. coli (see page 3973, column 1 discusses M13 origin of replication), and other sequences which can be of interest to someone, and where the vector is grown in the GM1690 E. coli host strain so that the vector lacks methyl adenine (see page 3973, column 2),

(b) a second DNA vector that is substantially complementary which has an mnt gene with an inactivating deletion of 5, 192, or 410 nucleotides and which comprises methyl adenine at GATC sites (see page 3973, columns 1 and 2, where the pPY97 vectors with the deletions are grown in the JC9239 E. coli host cell which results in methylated vector DNA (see page 3973, column 2).

(c) Carroway teaches competent host bacteria including GM4388, which is based on GM 4331 which is an MMR strain, where GM4388 has Tn5 which transposon has the antibiotic resistance Gene Kanamycin and which is inherently sensitive to other antibiotics (see page 3974, table 1).

With regard to claim 27, the pPY97 vector of Carraway comprises a selectable marker that is ampicillin resistance gene (see page 3974, column 2) and the pBR322 polylinker (see page 3973, column 1).

With regard to claims 28 and 29, Carraway teaches single stranded pPY mutant and wildtype (see page 3973, column 2).

With regard to claim 30, Carraway teaches annealing of the two vectors (see page 3973, column 2).

With regard to claims 31, 32, Carraway teaches competent host bacteria including GM4331 which is an MMR strain (see page 3973, columns 1 and 2, subheading "Bacterial strains").

With regard to claim 33, Carraway teaches the use of two oligonucleotides and the T7 DNA polymerase, which is "thermostable" as broadly interpreted (see page 3973, column 1).

Carraway does not teach the use of cre or flp as marker genes.

Zambrowicz teaches that a variety of genes can function as known equivalent markers, including antibiotic resistance genes, enzymes, fluorescent marker genes such as GFP and specifically cre and flp genes (see column 30, lines 40-49).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the cre or flp genes as markers in the kit of Carroway since Zambrowicz teaches that these markers are known as equivalent to the markers such as antibiotic resistance taught by Carroway. As MPEP 2144.06 notes " Substituting equivalents known for the same purpose. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion

to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout , 675 F.2d 297, 213 USPQ 532 (CCPA 1982)." Here, the prior art of Zambrowicz expressly teaches the equivalence of Cre and flp as markers with markers used in the prior art such as that of Carroway.

Response to Arguments

10. Applicant's arguments filed November 2, 2006 have been fully considered but they are not persuasive.

Applicant argues that the previous 102 rejections are moot. This argument is not persuasive since each of the references uses an MMR strain with antibiotic resistance genes and inherently comprises genes which do not provide antibiotic resistance. The specification does not define "antibiotic sensitivity genes", so any gene which is not "antibiotic resistant" may fall into that class.

Applicant argues the 103 rejection by first arguing that the elements are not equivalent. This is not persuasive since the elements are used in the same way for the same type of purpose, and are used in equivalent fashion by Zambrowicz. This is the essence of equivalence.

Applicant then argues advantages of the substitution, implying an unexpected result is present. This argument is not persuasive for two reasons. First, no comparative data is presented to demonstrate that the result is, in fact, unexpected. In fact, the result is precisely what is expected, since multiple selection elements are well known. With respect to the unexpected results argument itself, applicant's statement is

not evidence and the specification lacks comparative data. MPEP 716.01(c) makes clear that

> "The arguments of counsel cannot take the place of evidence in the record. In re Schulze , 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long - felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant."

Here, the statements regarding any potential unexpected results must be demonstrated, not simply argued.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Jeffrey Fredman
Primary Examiner
Art Unit 1637
12/4/06